Cancer rehabilitation

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6 The development of an evidence-based physical self-management rehabilitation programme for cancer survivors

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Submitted

Abstract

Objective The present paper describes the development of a physical training programme for cancer patients. Four related but conceptually and empirically distinct physical problems were described, including decreased aerobic capacity, decreased muscle strength, fatigue and impaired role physical functioning. The study aimed to identify the optimal content for an exercise programme that addresses the four physical problems, based on the highest level of evidence available. The study further aimed to review the evidence available on the delivery of the programmes. The last goal was to develop a programme in which content and delivery are based on the best available evidence.

Methods Literature searches (PUBMED and MEDLINE, to July 2006) on content looked for evidence on the efficacy of exercise on aerobic capacity, muscle strength, fatigue and impaired role physical functioning. Literature searches on delivery looked for individual and/or group approaches, local fitness and/or sport programmes, self-management and/or self-efficacy enhancing techniques in relation to outcome, adherence and/or adoption of a physically active lifestyle.

Results Evidence on the effectiveness of exercise varies and increases when moving from muscle strength (level of RCT), fatigue and physical role functioning to aerobic capacity (all level of meta-analyses). No evidence was found that differentiated between individual and group approaches, or between muscle strength training programmes and sports. There was some evidence (meta-analyses) that self-management programmes and self-efficacy enhancing programmes have beneficial effects on health outcomes in a variety of chronic diseases, on the quality of life in cancer patients, and on exercise adherence and later exercise behaviour.

Conclusion Evidence supports the positive effects of exercise on physiological, physical and psychological outcomes during and after completion of cancer treatment. Evidence supports the positive effects of self-management programmes and self-efficacy enhancing programmes on health outcomes, exercise adherence and later exercise behaviour.

Practice Implications The resulting programme was developed on the basis of the highest quality of evidence available regarding content and delivery. Potential advantages of the programme are: a) tailored physical training towards focusing on the patient's established problems; b) delivery of the training as a self-management programme that might have beneficial effects on health outcome, exercise adherence and a long-term physically active lifestyle.

Introduction

Due to improvements in diagnostics and treatment regimes, the survival rate of cancer patients is increasing. As a result, cancer is now considered to be a chronic disease and the attention paid to the quality of life of patients after cancer treatment is increasing. Approximately 30% of all survivors report a decreased quality of life due to physical and psychosocial problems following cancer and consequent treatment, and indicate that they need professional support [1] such as rehabilitation.

Physical training seems to be essential in the rehabilitation of cancer survivors. This is the case because, firstly, psychosocial interventions are less likely to improve physical and functional problems [2]. Secondly, physical training is reported to improve quality of life beyond the benefits of psychotherapy [3]. Thirdly, improvement in physical functioning following a rehabilitation programme is associated with a simultaneous decrease in fatigue [4]. Lastly, very recent studies reveal that increased physical activity after a cancer diagnosis reduces the risk of cancer recurrence and mortality [5,6].

Physical training should be aimed at reducing long-term physical problems. Physical side effects that occur during cancer treatment, such as anaemia, pain, nausea, vomiting and sleep disorders, may affect daily functioning and quality of life during that phase. Other physical and functional problems persist over time, including a decreased oxygen uptake, reduced muscle strength, fatigue and limited physical role functioning, and these continue to affect cancer patients' quality of life. Physical exercise has the potential to overcome such long-lasting problems [4,7,8].

These four problems, which are further discussed in Box 1, are to some extent interrelated, but appear to be empirically different. For example, aerobic capacity seems to be no different in Hodgkin's disease patients with or without chronic fatigue and it is therefore thought that aerobic capacity does not play a major role in the pathophysiology of fatigue [9]. Therefore, aerobic capacity and fatigue would require different physical training modalities. Although physical training programmes are commonly reported to be effective in improving aerobic exercise capacity and muscle strength, and in reducing fatigue and ameliorating physical role functioning [2,10,11], to date it is still unclear what type of exercise is most optimal in addressing each of the four defined problems. The optimal intervention modality, intensity, timing and duration are still unknown, despite the fact that there is growing evidence for the positive effects of physical training [12,13]. Standardized guidelines about the specific interventions are currently available for healthy individuals [14] but lacking for cancer patients. Until now, various programmes consisting of aerobic training, muscle strength training and/or flexibility training have been described for cancer patients, all with varying content [15].

In addition to the content, the efficacy of a physical training programme may depend on the delivery. However, no information is available concerning the best way to deliver a training programme for cancer patients. In that regard, the following approaches should be considered: an individual versus a group approach; a programme consisting of local exercise training or integrated exercises such as sport; and a traditional versus a self-management approach.

The choice of an individual or a group approach may depend on a number of issues. The efficacy of exercise may be higher if the training is personalized. However, the question could be asked whether personalized training should automatically imply individual training or whether a group approach is also applicable. A group approach might be preferred because peer contact provides opportunities for social support [16], social comparison [17] and modelling [18], validation, reappraisal and finding meaning [19]. Vicarious experiences among peers can also have positive effects on self-efficacy [20] which may in turn mediate physical [21] and mental health [22], and importantly, behaviour associated with physical activity [23]. In addition, social support processes seem to engender changes in lifestyle [24]. Finally, group programmes might be interesting because of cost-effectiveness.

Another point concerning delivery is the 'transfer' of local exercise training into daily activities. For example, muscle strength training may have significant positive effects on muscle strength and endurance and on physical functioning, but it is known that without the integration of functional training, improved muscle strength does not consistently result in improved functional task performance [25]. To undertake most daily activities an individual must be able to perform basic movements and also combinations of these in order to accomplish more complex tasks [26]. Sports such as indoor hockey, curling and badminton provide training in such complex tasks. Sports are often included in rehabilitation programmes to facilitate their integration into daily life, as it is more difficult to become physically active when sedentary [27]. Enjoyment of sport has also been reported to be a mediator for the adoption of an active lifestyle [28].

Finally, most physical training programmes are delivered in a traditional and therapist-oriented way, which means that the therapist prescribes the intervention and offers information and technical skills, while the patients follow these instructions [29]. However, managing the consequences of a disease such as cancer may require a patient-oriented intervention, characterized by active participation, taking personal responsibility and changing lifestyle [29,30]. Patient-oriented interventions such as self-management may include monitoring and managing symptoms, adherence to treatment regimes, maintaining a healthy lifestyle and managing the impact of the illness on daily functioning [30]. Self-management generally consists of six processes: goal selection, information collection through monitoring, information processing and evaluation (in relation to norms), decision-making, action and self-reflection [31]. In self-management, self-efficacy – which is a patient's own belief in his or her ability to perform specific actions or change specific thinking patterns and, thus, manage and minimize the symptoms – is believed to be of primary importance [20,29]. Self-management may have more beneficial effects than traditional interventions.

Self-management programmes may also be relevant to exercise adherence and for the adoption of a physically active lifestyle after the completion of a physical training programme [32]. A good level of adherence to an exercise regime may be a prerequisite for the effectiveness of exercise because a certain combination of duration, intensity and frequency per week is needed to improve aerobic fitness [14]. Prior studies reveal that adherence to and compliance with physical training programmes ranges from 52–89% [33], and underline the need to promote adherence to physical training regimes. It is important that patients adopt a physically active lifestyle after the prescribed training programme because low activity levels, which appear to be common in cancer patients [34], are associated with morbidity and mortality. Low level physical activity might also be considered as a maintaining cause for several of the physical problems discussed above, which means that low activity levels may induce a vicious circle of reduced oxygen capacity, lower muscle strength and more fatigue [35]. To improve exercise adherence and encourage the adoption of a physically active lifestyle, a structured exercise programme combined with theory-based behavioural interventions has been recommended [33].

Therefore, theoretical frameworks such as self-management [31] based on the self-regulation of behaviour [36], and self-efficacy stimulating techniques [20] based on social cognitive theory, may be relevant to exercise adherence and adoption, in addition to traditional physical training.

The aim of the present article is to describe the development of an exercise intervention that is designed to improve the four most relevant cancer-related physical problems (Box 1). Firstly, the literature will be reviewed for evidence regarding the content (such as modality and intensity) of the programme for each defined problem, and secondly for the evidence available regarding the three issues concerning delivery discussed above. Lastly, a programme will be presented in which content and delivery are based on the best available evidence.

Box 1

The most important and long-lasting physical problems in cancer patients

A *decreased maximal oxygen uptake* (VO_{2max}<20 ml/kg.min) is reported in about 13–30% of survivors after Hodgkin's disease [37;38] and non-Hodgkin's disease patients [38]. The physical performance of 70% of patients with solid tumours and haematological cancers is classified as 'poor' (50–54% of reference VO_{2max}) or 'very poor' (50% of reference VO_{2max}) [39]. A decreased oxygen uptake or aerobic capacity may reflect the difficulty the cardio-respiratory system has in delivering oxygen throughout the body and/or problems of the musculoskeletal system in extracting oxygen from the blood during aerobic exercise. Both radiotherapy and chemotherapy appear to have negative side effects on the cardio-respiratory system [7,40] and on the musculoskeletal system [35].

Significant muscle wasting and consequent *decreased muscle strength* [41] affects about 50% of persons with cancer [35;42-44]. Although the exact mechanisms are unclear, it is generally accepted that cancer-induced muscle wasting is a multifactorial process that is mediated by factors such as reduced energy intake, proinflammatory cytokines [9;44], accelerated muscle protein degradation and bed rest [8;35].

About 61-99% of cancer patients experience *fatigue* during and following cancer treatment [45-47]. Cancer-related fatigue, which is multidimensional in nature [48], might be caused by cancer-induced anaemia and tumour necrosis, but is also attributed to a reduced activity pattern as a consequence of prescribed bed rest [45,46]. Fatigue is associated with psychosocial problems such as anxiety and depression [49,50], reduced self-efficacy [51], sleep disorders, distress [45] and difficulty coping [44]. However, whether fatigue is a cause or a consequence of these factors is still unknown [48].

Many cancer patients report *reduced physical and reduced role functioning* due to physical problems [47]. Physical performance limitations, e.g. climbing stairs, walking short and long distances [52], were found to be significantly more prevalent among recent (54%) and long-term (53%) cancer survivors when compared to subjects with no cancer history (21%) [53]. Limitations in role functioning due to physical problems, such as reduced participation in social and sport activities [43,47], are reported in about 30% of both short and long-term cancer survivors, compared to 13% of subjects with no cancer history [53].

Methods

Our first aim was to review the evidence regarding the content of programmes that address the four physical problems mentioned in Box 1, based on the highest level of evidence available. A computerized search in PUBMED and MEDLINE (to July 2006) was conducted using the Mesh terms 'cancer', 'aerobic' and 'exercise capacity'. Additional searches were conducted using 'cancer', and 'muscle strength' and/or 'resistance training', and 'cancer' 'exercise' and 'fatigue'. 'Physical role functioning' is not a Mesh term but this broad term includes physical abilities that range from simple mobility to the engagement in complex activities that require adaptation to an environment. Thus, it includes objective and perceived mobility and participation in daily activities, which are important quality of life domains. Therefore, a search was conducted with 'cancer', 'exercise' and 'quality of life', and only the relevant physical domains were taken into account. All searches were limited to 'meta-analyses/systematic review' and 'English language'. When no meta-analyses/systematic reviews were found, the same Mesh terms were used and combined with 'Randomized Controlled Trials'(RCTs). When no RCTs were found, the same Mesh terms were used and combined with 'Clinical Trials'. Studies that focused only on exercise were included, while physical interventions combined with other interventions (such as diet or psychotherapy) were excluded. Controlled studies identified from meta-analyses that focused on the problems discussed above were taken into account. Furthermore, additional searches were performed to include controlled studies that were published after the RCTs included in the meta-analyses. If no studies of cancer patients were available, we searched for studies of other patient groups with chronic illness. We reviewed the evidence and analysed the content of the various programmes. If pre-intervention and post-intervention data were reported, we computed changes which were expressed as percentages of change from the baseline.

Our second aim was to review the evidence available on the delivery of the programme. A search in PUBMED and MEDLINE (to July 2006) was conducted using the following terms related to delivery: 'individual and/or group exercise', 'local exercise/fitness training and/or sports', 'self-management and/or self-efficacy' and 'adherence and/or physically active lifestyle', all combined with 'exercise and cancer'. All searches were limited to 'meta-analyses/systematic review' and 'English language'. When no meta-analyses were found, additional searches were performed with the same terms combined with 'Randomized Controlled Trials' and 'Clinical Trials'. If no studies were available for cancer patients, supplementary searches were performed using the same terms combined with other patient populations and/or the general population.

Results

Evidence concerning the content

Four meta-analyses [12,54-56] and two systematic reviews [13,57] on the effect of exercise and aerobic capacity, fatigue and quality of life in cancer patients were found. The meta-analyses and systematic reviews and additional controlled studies published after the meta-analyses revealed twelve relevant studies on exercise capacity [7,58-68], fourteen on fatigue [58,60,62,68-78] and nineteen on physical quality of life [58-60,63,64,67-69,71-81]. No meta-analyses or systematic reviews were found but nine randomized controlled studies reported on the effect of exercise training on muscle strength [63,66,77,79,80,82-85]. The controlled studies found are presented in Table 1.

Aerobic exercise capacity. The evidence for improvement in aerobic exercise capacity or oxygen uptake was found on the level of meta-analyses [56], with moderate weighted mean effect sizes (WMES) of .51 during and .65 after cancer treatment [12]. Further analyses of studies included in Table 1 revealed fairly consistent effects, which means that all but one showed positive effects on aerobic capacity. Due to variation in study populations, design and timing (during/after cancer treatment) and the relatively small number of studies, it was not possible to determine differences in effectiveness between the various programmes. With respect to the content it appeared that the programmes offered were quite similar. All programmes consisted of aerobic exercise modes such as cycling and walking [7,58-62, 64,65,67,68], and two programmes combined cardiovascular training with muscle resistance training [63,66]. Most programmes used a moderate to high aerobic training intensity with a training heart rate at 50-80% of the maximal heart rate (MHR), at 50–80% of VO2max or at 50–70% of the heart rate reserve (HRR), in line with the ASCM guidelines [14]. In most cases, a training volume of 10-30 minutes was used and frequency varies between three times weekly to daily.

Muscle strength. No meta-analyses or systematic reviews were found on the effectiveness of exercise on muscle strength in cancer patients. However, a systematic review that reported on the effect of progressive resistance exercise (PRE) on muscle strength in patients suffering from various other chronic diseases revealed moderate to large effect sizes [86]. For cancer patients, nine controlled studies (Table 1) were found that reported beneficial effects of aerobic exercise [83,85], PRE [77,80,84] or PRE in combination with aerobic exercise [63,66,79,82] on muscle strength. Because pre-intervention and post-intervention data were not available in five out of nine studies, it is not possible to determine differences in the effectiveness of the programmes. With respect to the content of the programmes it appeared that aerobic exercise consisted of walking or cycling with moderate to high intensity. PRE mostly consisted of the exercise of large muscle groups of the upper and lower extremities. Although the intensity of PRE should be based on the overload principle [14], weight settings were not precisely specified in most studies and varied from a fixed range of weights to the ability to lift weights until failure occurred in 8-20 repetitions. Only one study specified the intensity as moderate to high, based on 60-70% of 1-Repetition Maximum (1-RM) [77]. PRE was commonly performed in two to three sets with 8-12 repetitions per set. The majority of the sessions lasted 20-40 minutes with a frequency of two to four times weekly.

Fatigue. The evidence for reduction in fatigue was found on the level of meta-analyses [56] with a small weighted effect size of .11 [54], but a zero effect size was also reported [55]. This inconsistency and the rather small effect size might be attributed to the variety of programmes aimed at the reduction of fatigue. Regarding the content (Table 1), aerobic programmes were described with intensity varying from moderate to high (at 50–80% MHR, at 50–80%VO_{2max} or at 50–70%HHR) [58,60,69-72,75-78], to programmes that were self-paced [73,74] as well as programmes that were based on a 'rate perceived exertion' of 13-15 on the Borg Scale [62,68,87]. The latter two might be less intensive and aimed less at improvement of aerobic capacity than the first programmes. However, based on the studies included, no differences in effectiveness could be determined, although a frequency of at least three times a week seemed to be associated with a positive effect on fatigue. In addition, one study reported positive effects of progressive resistance exercise on fatigue [77]. One study comparing aerobic training combined with PRE to placebo reported no significant differences in fatigue between the groups [72]. One study comparing aerobic exercise and relaxation reported equal beneficial effects on fatigue without differences between the groups [62]. The last aerobic training study reported no beneficial effect on fatigue, despite an improvement in VO_{2max}, and attributed this to an overly high training intensity (60–70% MHR)[68]. Thus, regarding fatigue, aerobic exercise may be beneficial but a high intensity does not seem necessary or may even have negative effects. The results may support the need for further research. Perhaps the multidimensional nature of fatigue requires other approaches, which is supported by a systematic review of the management of chronic fatigue syndrome that concluded that graded exercise therapy and cognitive behavioural therapy showed the most promising results [88].

Quality of life/Physical role functioning. The evidence for the improvement of quality of life in cancer patients was found on the level of meta-analyses [56] with a weighted effect size of .30 [12,54]. These effect sizes may be due to inconsistent findings across the various studies and/or variety in the content of the programmes. Table 1 shows that both aerobic exercise programmes with a moderate training intensity [59,60,64,67,75-78] and self-paced programmes [73,74] were effective in increasing physical role functioning. Another study, using low and moderate aerobic exercise, found beneficial effects on physical wellbeing, despite a lack of effect on aerobic capacity [58]. One study found that stretching exercises with no resistance training may be feasible for improving physical well-being [71]. Interestingly, one aerobic training study reported that despite physiological improvement, no beneficial effect on quality of life, including physical functioning, occurred within the exercise group [68], and this was attributed to an overly high training intensity. Furthermore, programmes with a combination of aerobic exercise and PRE [63,69,79,81] or PRE alone [77,80] also showed beneficial effects on physical role functioning, except one [72]. Thus, with respect to physical functioning, aerobic exercise and/or PRE may have beneficial effects. However, there are inconsistencies in the intensity of the programmes, varying from low to moderate intensity, and one study argues against a high intensity. Lastly and importantly, improvement in physical function may be independent of an increase in aerobic capacity.

With respect to all the problems defined and the studies included in Table 1, some overall findings were determined. In general, many programmes were offered under supervision or at home, and many used exercise logs. Both cycling and walking programmes were used, of which cycling may be the safest as it is a non-weight-bearing exercise [14]. The length of training programmes varied between three weeks and six months. Most studies presented used breast cancer patients, but positive findings were also found in patients with other types of cancer, such as leukaemia, stomach, prostate, colorectal and ovarian [15]. This may indicate that exercise is effective in a variety of cancer types. Furthermore, exercise is shown to be effective during and after completion of cancer treatment – both preventing deterioration and improving physical functioning.

Summary and conclusion concerning the content

Although several studies were limited, using a small sample size (Table 1) and having insufficient reports on the methodological criteria, many studies support the positive effects of exercise on physiological, physical and psychological outcomes during and after completion of cancer treatment. However, the level of evidence on the effectiveness of exercise on the reduction of physical problems varies according to the defined problem, and evidence increases when moving from muscle strength, fatigue and physical role functioning to aerobic capacity.

Concerning the content, two modalities of exercise are commonly described: aerobic exercise training and PRE. Aerobic training seems to have beneficial effects on aerobic capacity, fatigue and physical role functioning. PRE alone or combined with aerobic training may have a beneficial effect on muscle strength, fatigue and physical role functioning. Regarding the intensity, training programmes with a moderate to high intensity seem to be effective in improving aerobic capacity and muscle strength. Concerning reduction of fatigue and the improvement of physical role functioning, findings are not consistent and some argue against a high training intensity. Furthermore, aerobic training (cycling or walking) alone or combined with PRE seems to be effective and applicable to all defined problems.

Evidence concerning the delivery

Individual versus group programmes. No meta-analyses or RCTs were found that focused on differences in effect between individual or group exercise programmes. Literature on interventions other than physical exercise is divided regarding the relative merits of individual versus group therapy. One meta-analysis on the effect of cognitive behavioural therapy in breast cancer patients reported that individual treatment approaches had significantly larger effects on distress ($p=0.04$), but not on pain ($p > 0.05$) [89], than did group approaches. Another meta-analysis that examined the effect of psychological interventions on anxiety and depression in breast cancer patients concluded that group therapy is at least as effective as individual therapy [90]. A meta-analysis of self-management in diabetes showed that lifestyle interventions were generally more effective in group settings, whereas skills teaching was effective in individual and group settings [91]. In sum, evidence concerning the effects of individual as compared to group-based approaches on exercise is lacking, but most results in other interventions point out that conducting group programmes is feasible and effective. Based on the RCTs on exercise in cancer patients (Table 1), it is not possible to draw conclusions about the efficacy of group versus individual exercise because most studies do not specify the intervention as such. Most studies specify their intervention as home-based, which is most likely to be individual, or as supervised, which can be tailored to either the individual or a group. Two RCTs reported on the beneficial effects of *a group exercise* programme in cancer patients [62,69], and one of these considered that the effects of the programme may be attributed to the presence of support provided by peers [69]. An RCT comparing a group exercise programme and individual physiotherapy for back pain reported no significant differences in efficacy but suggested lower costs for the group programme [92].

Local exercise/fitness training versus sports. No meta-analyses or RCTs were found that focused on comparing the effectiveness of local exercise/fitness and sport in cancer patients or in other patient groups. An RCT on healthy elderly women reported that functional-task exercises were more effective than progressive muscle strength training at improving functional task performance [25]. RCTs in muscle strength training in cancer patients (Table 1) showed beneficial effects on muscle strength and on physical functioning. Regarding sports, an RCT on rehabilitation programmes for patients who suffered a stroke or had neurological or back disorders reported beneficial physiological alterations after sport such as cycling, tennis and jogging compared to the control group [27]. A Cochrane review reported that playing sport might have a favourable effect on physical activity levels and physical health, help develop sport-specific skills, provide a sense of achievement and empowerment, develop self-esteem and teach self-discipline [93].

Self-management/self-efficacy interventions and effectiveness, adherence to exercise, and adoption of physically active lifestyle. A search on the effectiveness of self-management and self-efficacy in cancer patients revealed one meta-analysis. This meta-analysis of social cognitive theory, including components addressing self-efficacy, expectations and self-regulation, showed that psychosocial interventions including these components had greater effects on quality of life in cancer patients than interventions that involved fewer or no social cognitive theory components [94]. Additional searches on the effectiveness of self-management approaches as compared to controls and/or to routine care in other chronic diseases revealed eleven relevant meta-analyses which support the notion that self-management programmes are beneficial in controlling and preventing chronic disease complications. Self-management programmes appeared to have beneficial effects on health outcomes in diabetes [95-100], hypertension [95,101], cardiac [102], asthma/COPD [98,103,104] and arthritis [105] patients. However, no effect of self-management was reported in meta-analyses of osteoarthritis [95] and arthritis [98]. Most evidence suggests that self-management programmes and self-efficacy enhancing techniques are more effective compared to no intervention, and some evidence suggests that self-management is more effective compared to traditional care programmes.

Adherence to and efficacy of exercise showed a linear dose response relationship; the higher the adherence the greater the efficacy of exercise [106]. It has been reported that two weekly sessions are needed to maintain and three to improve aerobic fitness [14]. Because adherence and compliance to physical training ranges from 52-89% [33], in traditional interventions some experiments have been reported concerning variations in exercise prescription. One RCT compared adherence to aerobic exercise prescription with two levels of intensity (45-55% and 65-75% HRR) crossed with two levels of frequency (3-4 versus 5-7 days per week). A higher frequency seemed associated with an accumulation of exercise without a decline in adherence, whereas prescribing a higher intensity decreased adherence and resulted in the completion of fewer exercises [107]. Regarding adherence in weight training, a twice-weekly weight training programme under supervision appeared to be behaviourally feasible and effective in the short and long term [108]. In addition to exercise prescription, self-management programmes or self-efficacy enhancing techniques may also be relevant for adherence to and adoption of exercise. Self-management theory considers internal motivation as more effective for lifestyle change than external motivation (that is, 'changing to please the physician') [29]. The importance of self-efficacy for initiating and maintaining regular physical activity derives from social cognitive theory [20] and underlines the fact that efficacy beliefs are critical to the success in short-term structured exercise programmes due to their effect of enhancing adherence [109].

No meta-analyses were found on self-management/self-efficacy interventions related to exercise adherence and the adoption of a physically active lifestyle in cancer patients. One meta-analysis of cardiac patients revealed that self-management strategies were promising in improving cardiac rehabilitation uptake, adherence and/or lifestyle changes [102]. It was noted that performance self-efficacy seems to be more important in the early adoption phase of a clinical exercise programme, whereas self-regulatory skills are more important in the maintenance phase of exercise. This is in line with two meta-analyses of healthy elderly people, revealing that physical activity may lead to mastery experiences that can increase the level of self-efficacy [110], which may in turn have a moderating and positive effect on physical activity [28]. A third meta-analysis using the Trans-Theoretical model (TTM) of behaviour change revealed that changes in self-efficacy were moderately consistent with the predictions of TTM in the physical activity domain. Thus, self-efficacy was associated with exercise behaviour [111]. In colorectal cancer patients, an RCT reported that programmed exercise and perceived success – which can elevate levels of self-efficacy – were predictors of post-programme exercise [112]. Two RCTs also found that self-efficacy was a mediator of later physical activity in cardiac patients [113] and healthy elderly people, and the latter study additionally reported that two dimensions of self-efficacy were important for exercise adherence: the level of self-efficacy at baseline and the amount of change in self-efficacy [23].

Because behavioural changes, such as developing a physically active lifestyle, may require that adequate perceptions concerning the illness already exist, we performed an additional search on illness perceptions. The notion of illness perceptions is derived from the self-regulation theory that proposes that individuals construct schematic representations of illness [114]. Such representations or perceptions include five related but conceptually and empirically distinct components: identity (label and symptoms), timeline, cause consequences and curability/controllability. One meta-analysis of diverse patient populations revealed that a stronger perception of identity, timeline and consequences was associated with passive coping and lower functioning [115]. In contrast, patients who perceived high controllability seemed to have more active coping styles and better functioning than those with perceived low controllability [115]. Furthermore, several RCTs reported the beneficial effects of therapeutically manipulated illness perceptions on coping and quality of life in patients with myocardial infarction and cardiac surgery patients [116].

Conclusion concerning the delivery

Regarding the delivery, no evidence was found that differentiated between individual and group approaches, or between muscle strength training programmes and sports. There was some evidence that self-management programmes and self-efficacy enhancing programmes have beneficial effects on health outcomes in a variety of chronic diseases, on the quality of life in cancer patients, and on exercise adherence and later exercise behaviour.

Presentation of the programme

Guided by the conclusions concerning the content and the delivery we developed a physical training programme. In the present section we will describe the programme in general terms. Appendix I describes the programme in more detail, including information on the treatment elements during the various phases of the programme.

Based on the conclusions regarding the *content* of the programme we developed a supervised exercise programme, consisting of four separate modules tailored to the individual patient's most prominent problem. These modules are formulated in terms of individual goals: 1) improvement of aerobic capacity, 2) improvement of muscle strength, 3) reduction of fatigue, and 4) improvement of role functioning. The four modules contain two personalized treatment modalities including aerobic exercise training and PRE, which differ in intensity depending on the problem. The intensity of the programme is moderate to high in modules 1 and 2 and low to moderate in modules 3 and 4. The intensity of aerobic exercise and the PRE is prescribed on the basis of the MHR and the 1-RM in line with the ASCM guidelines [14]. With respect to aerobic exercise training, we chose a cycling programme because it is non-weight-bearing and, therefore, the safest exercise mode. PRE includes various exercises for the large muscle groups of the lower and upper extremities using machine resistance and/or free weights. Training sessions are 20-30 minutes duration for the aerobic cycling programme and 10–20 minutes duration for the PRE. The entire programme takes 12 weeks.

Based on the results regarding the *delivery* we adjusted the programme along the following lines. Acknowledging the value of personalized exercise programmes, recognizing the potential advantages of group therapy, such as social support and modelling, and based on considerations of cost-effectiveness, we developed the physical training programme as a group programme in which the individual is able to work towards his or her own goals. Thus, the group as a whole performs aerobic exercise and progressive muscle strength training, but the individual exercise modules are tailored to individual problems and are therefore prescribed individually. Based on the potential advantages of sport we included group sports in addition to individual aerobic exercise training and progressive resistance exercises.

Regarding the results on adherence and exercise prescription, we chose to deliver the cycling exercise programme and the PRE twice a week under supervision, and extended this with an aerobic home-based walking programme that allows for an increase in the frequency from once a week to daily. In addition, due to the evidence suggesting that self-management programmes and self-efficacy enhancing programmes have beneficial effects on functioning in chronic diseases, on quality of life in cancer patients, and on exercise adherence and later exercise behaviour, we integrated self-management and self-efficacy enhancing techniques into the programme. Because self-efficacy is enhanced through mastery experiences (perceived success in fitness), vicarious experiences (modelling), verbal persuasion (therapist) and physiological feedback (such as a decreased heart rate) [20], these sources are systemically manipulated during the aerobic exercise training, the PRE and the sports undertaken. Self-management is integrated into the programme by including the six processes of self-management [31] in the physical exercise programme and sport. These were *goal setting*, which seems to fulfil a crucial role in rehabilitation [117] and is an important determinant of actual performance, motivation for change, and improving self-efficacy in specific situations [94,118]; followed by *information collection* through self-monitoring (for example, checking heart rate, scoring Borg Scale and Visual Analogue Scale); *information processing and evaluation*, involving detection of change, and evaluation of information against norms such as heart rate or Borg Scale; *decision-making action*, the actual performance of self-management skills such as exercise; and *self-reaction*, the evaluation of performance by providing feedback [31]. In addition, we included attention to illness perceptions during the programme because rational perceptions were considered to be a prerequisite for active coping and behavioural change.

Discussion

The present paper describes the development of a physical training programme for cancer patients. Four related but conceptually and empirically distinct physical problems were described, including decreased aerobic capacity, decreased muscle strength, fatigue and impaired role functioning, all probably the result of low physical activity. The paper aimed to identify the optimal content for an exercise programme that addresses the four physical problems, based on the highest level of evidence available. Although several studies were limited, using a small sample size and having insufficient reports on the methodological criteria, many studies support the positive effects of exercise on physiological, physical and psychological outcomes during and after completion of cancer treatment. However, the level of evidence on the effectiveness of exercise on the reduction of physical problems varies according to the defined problem, and evidence increases when moving from muscle strength (level of RCT), fatigue and physical role functioning to aerobic capacity (all level of meta-analyses). The paper further aimed to review the evidence available on the delivery of the programmes. The study revealed no evidence that differentiated between individual and group approaches, or between muscle strength training programmes and sports. There was some evidence (meta-analyses) that self-management programmes and self-efficacy enhancing programmes have beneficial effects on health outcomes in a variety of chronic diseases, on the quality of life in cancer patients, and on exercise adherence and later exercise behaviour.

Conclusion

Evidence supports the positive effects of exercise on physiological, physical and psychological outcomes during and after completion of cancer treatment. Self-management programmes and self-efficacy enhancing programmes seem to have beneficial effects on health outcomes in a variety of chronic diseases, on the quality of life in cancer patients, and on exercise adherence and later exercise behaviour.

Practice Implications

The resulting programme was developed on the basis of the highest quality of evidence available regarding content and delivery. Potential advantages of the programme are:
a) tailored physical training towards focusing on the patient's established problems;
b) delivery of the training as a self-management programme that might have beneficial effects on outcome, adherence and a long-term physically active lifestyle. A randomized controlled trial (the Oncorev study) is currently ongoing and designed to examine the effectiveness of the physical training programme on exercise capacity, muscle force, fatigue and physical role functioning.

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Appendix I: A detailed description of the programme: phases and treatment ingredients

The self-management and tailor-made physical training programme is preceded by a physical *assessment*, which defines a patient's problems and needs by assessing exercise capacity (Symptom Limited Bicycle Ergometry, SLBE) [119], testing muscle strength (1-RM test) [120] and anamnesis. The SLBE is considered to be the most precise measure of cardio-respiratory fitness and is recommended for use in order to determine a patient's objective or subjective reduction in exercise capacity and prescribe the intensity of the aerobic bicycle training programme [14]. An 1-RM test is performed to determine maximal muscle strength as an indicator of the intensity of the progressive resistance exercise [14]. Additional information about the patient's reduction in exercise capacity, functioning and activity pattern is obtained by an extended anamnesis, to establish whether and to what extent a patient suffers from the following: decreased aerobic capacity, reduced muscle strength, fatigue or limited physical role functioning. The anamnesis further includes exploration of the presence of irrational illness perceptions [115], and the patient's expectations and goals [117] according to the self-management approach.

Before the exercise programme starts, an *education session* is held to acquaint the patient with peers, therapists and the therapeutic surroundings. Patients are informed about the programme's rationale of physical training, self-management processes [48] and illness perceptions. Patients are told that physical training has the potential to break through the vicious circle of physical cancer-related problems [15], and that self-management considers the patient's responsibility to be central, whereas the role of the therapist is that of a guide. Patients have to commit themselves to this approach [31] and are invited to define their self-management goals as a necessary condition for behavioural change [30]. Finally, it is explained to the patient that rational illness perceptions [121] are the prerequisite for adequate and active self-management behaviour, and they are asked to explore their perceptions [115].

In the *tailoring* phase, the intervention is divided into an Individual Physical Training (IPT) programme and a group-oriented Sports and Games (SGP) programme, both supervised by a physical therapist. The IPT includes four individual modules tailored to individual problems and consists of improvement of 1) oxygen uptake/aerobic capacity, 2) muscle strength, 3) fatigue, and 4) physical role functioning. The four modules all use aerobic bicycle exercise training and progressive resistance training, which differ in intensity. The aerobic training is based on the maximal heart rate reached during the SLEB test. The training heart rate (THR) is computed by using the Karvonen formulae [122]. Progressive resistance muscle training of the trunk and the lower and upper extremities are performed and is based on the individual 1-RM [123].

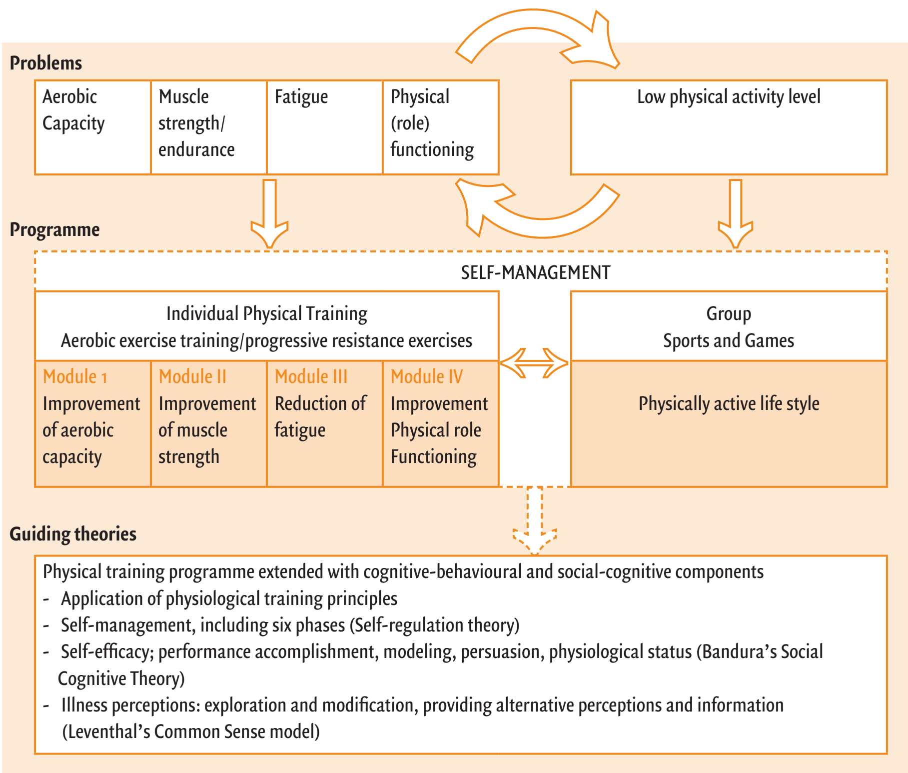
The first four weeks of the IPT are used to verify the patient's main problem defined at intake and their physiological response to training [14] in order to establish the most optimal training module. The aerobic training is performed at a THR of HRrest + 30-50% (HRmax–HRrest) over 20 minutes. Progressive resistance muscle training starts at 30% of the 1-RM, with a frequency of 10–20 repetitions over three series. Illness perceptions are individually explored and their effect on active behaviour is generally discussed in the group. Two processes of self-management are practiced, including goal setting [94,124]and monitoring [31]. Goals should be self-generated and positively formulated, otherwise motivation will fade [30]. Therefore, patients are invited to set specific, measurable, adequate, realistic and time-related (SMART) goals. Monitoring includes measuring the heart rate, scoring the Borg Scale for fatigue and dyspnoea before and following exercise, and using an exercise log. Successful performance accomplishment as a source of self-efficacy [20,125] is achieved by a low training intensity in the first four weeks, providing the opportunity for all patients to perceive success.

During weeks five to twelve aerobic bicycle exercise training continues at a THR of HRrest + 50-80% (HRmax–HRrest). The progressive resistance training increases from 30% of the 1-RM by 5–10% up to 50-65% of 1-RM. Intensity and progression of both training modalities differ between modules and are moderate to high in modules 1 and 2, and mild to moderate in modules 3 and 4. Training sessions are 30-45 minutes long with 20-30 minutes of aerobic training and 10-15 minutes of muscle resistance training. Patients are advised to have at least one additional aerobic training session a week, using a home-based walking programme. The walking programme [126] starts in week six with 5–10 minutes walking, which increases to 20 minutes by the end of rehabilitation. Furthermore, all six processes of self-management are included in each module. Thus, in addition to goal setting [124,127] and monitoring, patients evaluate their scores against the norm provided [31], and undertake action in the form of physical training applied to their problem [15]. Finally, self-reflection [31] is accrued by visual and oral feedback, such as graphics combined with reflective questions by the physical therapist.

Irrational illness perceptions which are revealed in weeks one to four are challenged by providing information, raising doubt, and providing alternative perceptions [116]. Information about the application of physiological training principles in cases of cancer-related problems is provided to all patients so as to change irrational perceptions about exercise and cancer. Patients with fatigue as their main problem (module 3) further receive an illustrative 'model of fatigue' that explains fatigue as a multidimensional construct with different physical and psychological determinants [4]. These patients are encouraged to undertake physical activity to increase their exercise capacity gradually without 'centralizing' fatigue, which may be considered as a cognitive behavioural technique of the therapist. Patients who have problems with role functioning (module 4) are taught how to restore the balance between 'demand' and 'capacity' during tasks and activities [128]. Exercise is combined with information about the 'demand and capacity model' in order to reach a better understanding of methods to reduce 'demand' by reducing activities that cause fatigue, and to increase the 'capacity' by graded exercise [15,129]. Finally, self-efficacy enhancing techniques are applied, such as a patient's perceived mastery experiences, a therapist's verbal persuasion, and vicarious experiences of peers regarding the ability to perform exercise tasks and recognize an improved physiological status such as a decrease in heart rate during exercise [20,125].

The GSP includes twenty-four one-hour sessions over twelve weeks with various sports and games such as indoor hockey, curling and badminton that stimulate patients to engage in and to enjoy sports, both aimed at improvement through a physically active lifestyle. In line with the IPT, the GSP is based on a self-management approach. Patients are invited to set SMART goals alongside the overall goal of increasing their activity level during leisure time [124,127]. Patients complete a Visual Analogue Scale to monitor their level of enjoyment during sport or games [31]. Action is fulfilled through the actual engagement in sport and games. Self-reflection is stimulated through reflective questions by the therapist. The GSP also includes, if necessary, attention to irrational perceptions [121] that may be barriers to the adoption of an active lifestyle. Furthermore, the GSP module has a fixed structure, including warming-up, main part and cooling down, aimed at an increase in self-efficacy [20]. During warming-up, basic elements of the sports that will be performed during the main part are practised. The main part contains the actual sport performance and uses already learned movements in the sport and game activities, allowing patients to perceive success more easily. Peers are invited to engage in sport together so that modelling experiences may occur. Therapists guide these processes and use verbal techniques to persuade patients to engage in sport or games. Afterwards a cooling-down period takes place using relaxation techniques to lower physiological arousal [20].

Overview of the relationship between physical problems in cancer patients, the proposed programme and guiding theories of the programme. Patient's main problems including a decreased aerobic exercise capacity, loss of muscle strength, fatigue or limited physical role functioning. The low activity level is considered the maintaining factor. The individual training module is tailored to the individual problems. The Group Sports and Games are tailored to the adoption of a physically active lifestyle



Overview of the programme including an assement phase to determine patient's main problems and needs, an educational phase to explain the programme rationale, and a tailoring phase in which the physical training is tailored to the patient's needs. The tailoring phase (12 weeks) consits of two self-management programmes: an Individual Physcal Training and Group Sport and Games. Tailoring is achieved by applying physiological training principles, exploring and changing individual irrational illness perceptions, self-management phases, and stimulating self-efficacy

Phase	*Assessment*		*Education*	*Tailoring*				
Structure/ modalities	Intake		Introduction session	Physical training programme				
Content	SLBE test Muscle test Anamnesis		Acquaintance Education and Information about programme rationale including exercise, self-management, and illness perceptions	Self-management				
				Individual Physical Training				Group Sport and games
				Aerobic capacity	Muscle strength	Fatigue	Role Functio-ning	Physically active lifestyle
Weeks	-2	-1	0	1-12				
Frequence Time/hour	1/1	1/1	1/2	2x0.75 for 12 weeks = 18 hours				2x1for 12 weeks = 24 hours
Aims	To define patient's main physical problem To explore irrational perceptions To prepare self-management expectancies		To acquaint patient with peers, therapists, and surrounding To increase knowledge To divide roles between patient and therapist	Tailor-made exercise training to reduce patient's main physical problem To change irrational perceptions To increase self-management, exercise adherence and adoption of exercise in the longer term To enhance self-efficacy				To perform and to increase enjoyment in various sports and games To increase self-efficacy and self-management in order to inspire a physically active lifestyle

Table 1

Description of controlled studies of physical exercise on exercise capacity, muscle strength, fatigue and physical functioning

Study	During/after treatment	Type of cancer	Type of exercise programme	Intensity (load)	Frequency, volume, duration	Number of patients	Outcome
I) Effectiveness on oxygen uptake/aerobic capacity/maximal exercise performance							
Burnham 2002 [58]	After surgery, radiation, surgery	Breast and colon cancer	Low intensity aerobic exercise Moderate-high intensity exercise Treadmill and cycling	25–40% HRR 40–60% HRR	3/week 14–32 minutes 10 weeks	21	No differences between low and high intensity Combined groups showed significant increase in VO2max in EG (18.6%) compared to CG (2.7%)
Courneya 2003 [59]	After surgery, receiving adjuvant therapy	Colorectal	Home-based aerobic exercise Walking and cycling	50–75% MHR	3–5/week 10–30 minutes 16 weeks	102	No differences between groups with respect to cardiovascular fitness
Courneya 2003 [60]	After surgery, radiation and chemo-therapy	Breast	Supervised aerobic exercise Cycling	70–75% VO2max	3/week 15–35 minutes 15 weeks	53	14.5% increase in VO2max in EG and a decrease (-3%) in (W)CG
Dimeo 1997 [7]	During chemotherapy and autologous PBSCT	Mixed solid tumours	Supervised aerobic exercise Cycling on bed ergometer	50% HRR (220-age-resthr)	Daily 15–30 minutes during hospitali-zation	70	Loss of maximal performance was 27% higher in CG compared to EG EG had significantly higher scores on maximal performance compared to CG, data NA
Dimeo 1997[61]	After chemotherapy and autologous PBSCT	Mixed solid tumours and non-Hodgkin's	Supervised interval-endurance exercise Treadmill walking	80% MHR (calculated)	5 week 3–30 minutes 6 weeks	32	Increase in maximal performance (speed) in EG (34%) was significantly higher compared to control (21%)

I) Effectiveness on oxygen uptake/aerobic capacity/maximal exercise performance

Study	During/after treatment	Type of cancer	Type of exercise programme	Intensity (load)	Frequency, volume, duration	Number of patients	Outcome
Dimeo 2004 [62]	After surgery	Lung and gastro-intestinal cancer	Aerobic exercise group versus relaxation group	80% MHR/ Borg 13-14	5/week 15–30 minutes 3 weeks	69	EG showed 8% increase in maximal performance, no change in RG
Herrero 2006 [63]	After surgery and radiotherapy	Breast	Supervised aerobic exercise Cycling on ergometer Resistance training	70–80 % MHR Weight that allowed 12–15 repetitions, than adjusted to 8–10 repetitions, followed by an increase of 5–10%	3/week 70 minutes (20–30 minutes aerobic) 11 exercises 8–15 repetitions, 3 sets 8 weeks	16	EG showed an increase in VO_2max (9%) and a decrease in CG (-6%)
Kim 2006 [64]	During chemotherapy or radiotherapy	Breast	Supervised aerobic exercise Cycling, walking, running	60-70% VO_2 max	3/week 30 minutes 8 weeks	41	EG showed significant increase in VO_2max (8%), no significant changes in CG (2%)
MacVicar 1989 [65]	During chemotherapy	Breast	Supervised aerobic interval exercise; alternating higher and lower intensity Cycling	60–85% HRR	3/week, 20–30 minutes 10 weeks	49	VO_2max and maximum work-load improved in EG (40%) compared to placebo (stretching exercises) and to CG

I) Effectiveness on oxygen uptake/aerobic capacity/maximal exercise performance							
Study	During/after treatment	Type of cancer	Type of exercise programme	Intensity (load)	Frequency, volume, duration	Number of patients	Outcome
Nieman 1995 [66]	After surgery, chemo-therapy radiotherapy	Breast	Supervised cardiovascular exercise Walking Resistance training	75% MHR Weight unspecified	3/week 30 minutes, 7 different exercises 12 repetitions 8 weeks	16	Modest improvement in aerobic capacity EG; walking distance increased significantly in EG compared to CG, heart rate tended to be reduced, data NA
Segal 2001 [67]	During radiotherapy, chemotherapy hormonal therapy	Breast	Cardiovascular exercise self-directed Walking versus supervised programme and usual care	50–60% VO2max	5/week self-directed group 3/week supervised group, 2 days at home No specification of volume 26 weeks	123	≈ Vo2 max in CG, and increased 3.5% in self-directed group and 2.5% in supervised group (NS) Supervised exercise showed significantly more increase in VO2 compared to usual care and to self-directed group only in patients not receiving chemotherapy
Thorsen 2005 [68]	After chemotherapy	Mixed cancer diagnosis	Supervised home-based aerobic programme Walking and cycling	Borg on 13–15 60–70% MHR	Minimal 2/week, more were allowed At least 30 minutes 14 weeks	139	23% increase in VO2 max in EG, and 10% in CG

II) Effectiveness on muscle strength

Study	During/after treatment	Type of cancer	Type of exercise programme	Intensity (load)	Frequency, volume, duration	Number of patients	Outcome
Coleman 2003 [82]	During chemo-therapy and stem cell transplantation	Multiple myeloma	Home-based aerobic exercise Walking Strength resistance training	12–15 Borg Muscle training with stretch bands with 2–27 lbs of resistance	3/week 18 minutes 4 sets of strength training 6 months	24	Significant increase in lean body mass in EG compared to CG Increase in muscle strength in EG and a decrease in CG (ns), data NA
Hayes 2003 [79]	After chemotherapy and PBSCT	Mixed cancer diagnoses	Aerobic exercise Treadmill walking and cycling Resistance exercise	70–90% MHR Weight set to induce failure between 8–20 repetitions in large muscle groups	3/week 20–40 minutes 3–6 exercises 2/week, no specification of sets 3 months	12	Fat free mass increased significantly in exercise group and not in CG, data NA
Herrero 2006 [63]	After surgery and radiotherapy	Breast	Supervised aerobic exercise Cycling on ergometer Resistance training	70–80 % MHR Weight that allowed 12–15 repetitions, than adjusted to 8–10 repetitions, followed by an increase of 5–10%	3/week 70 minutes (20–30 minutes aerobic) 11 exercises 15 repetitions, 3 sets 8 weeks	16	Significant effect of group and time in total muscle mass; EG showed an increase in muscle mass (3%) and a decrease in CG (-1%) Significant effect of group and time for leg press and sit-stand test, but not for bench press

II) Effectiveness on muscle strength

Study	During/after treatment	Type of cancer	Type of exercise programme	Intensity (load)	Frequency, volume, duration	Number of patients	Outcome
Nieman 1995 [66]	After surgery chemo-therapy radiotherapy	Breast	Supervised cardiovascular exercise Walking Weight training	75% MHR Increase of weight not specified	3/week 60 minutes 8 weeks 2 sets 12 repetitions 7 exercises	16	Leg extension strength tended to increase more in EG compared to CG, (ns) data NA
Mello 2003 [83]	After bone marrow transplant	CML, AML, NHL, MDS	Interval aerobic exercise Walking Active range of motion exercises/muscle stretching	70% MHR	Daily 40 minutes 6 weeks	32	EG showed higher values for all muscle groups compared to CG Exercise group increased for 3 of 8 (UE) and 5 of 10 muscle groups (LE), data NA
Ohira 2006 [80]	After radiotherapy surgery chemotherapy	Breast	Supervised weight training followed by self-directed weight training Comparison EG with delayed group	Resistance machines and free weights not specified	2/week 9 exercises 26 weeks	86	Changes in bench press were 63% in EG versus 12% in delayed group Leg press 1-RM increases were 38% versus 9% for delayed group
Schmitz 2005 [84]	After radiation, chemotherapy	Breast	Supervised weight training followed by self-directed with training, comparison with waitlist controls	No weight for upper extremity Weight for lower extremity based on the ability to lift 8–10 times	2/week 60 minutes 3 sets 8–12 repetitions. 12 months: 6 months supervised, 6 months maintenance WCG from months 7 to 12	85	Significant increase in lean muscle mass (2.3%) compared to controls (no change)

II) Effectiveness on muscle strength

Study	During/after treatment	Type of cancer	Type of exercise programme	Intensity (load)	Frequency, volume, duration	Number of patients	Outcome
Segal 2003 [77]	During hormone therapy	Prostate	Supervised resistance exercise	60–70% of 1-RM increase of 0.5 lb when >12 repetitions were completed	3/week 2 sets 8–12 repetitions 9 exercises 12 weeks	155	EG showed higher levels of upper (40%) and lower body (32%) muscular fitness compared to WCG (-8% and -4%, respectively)
Winningham 1989 [85]	During adjuvant chemotherapy	Breast	Supervised cycle interval protocol	60–85% VO_2 max	3/week, 20–30 minutes 10 weeks	24	Increase of lean mass in EG compared to controls, data NA

III) Effectiveness on fatigue

Study	During/after treatment	Type of cancer	Type of exercise programme	Intensity (load)	Frequency, volume, duration	Number of patients	Outcome
Burnham 2002 [58]	After surgery, radiation, surgery	Mixed	Low intensity aerobic exercise Moderate-high intensity exercise Treadmill and cycling	25–40% HRR 40–60% HRR	3/week 14–32 minutes 10 weeks	21	Fatigue decreased in EG but not differing significantly from CG
Campbell 2005 [69]	During adjuvant chemotherapy/radio-therapy/combined	Breast	Supervised aerobic training Walking and cycling Muscle strengthening exercises	60–70% MHR(age adjusted) Muscle strengthe-ning not specified	2/week 10–20 minutes 12 weeks	22	No significant differences in fatigue between EG and CG
Courneya 2003 [60]	After surgery, radiation, chemo-therapy	Breast	Supervised aerobic exercise Cycling	70–75% VO2max	3/week 15–35 minutes 15 weeks	53	Significant reduction in fatigue in EG (53%) compared to CG (19%)
Dimeo 1999 [70]	During chemotherapy	Mixed solid tumours, heamato-logical	Supervised aerobic exercise Biking on a bed ergometer	50% HRR interval Mean workload 30 (±5) Watt	Daily 15 to 30 minutes with rest of 1 minute Unspecified duration	63	Fatigue in EG remained unchanged and increased (25%) in CG during hospitalisation
Dimeo 2004 [62]	After surgery	Lung and gastroin-testinal	Aerobic exercise group versus relaxation	80% MHR/ Borg 13-14	5/week, 15–30 min 3 weeks	69	Fatigue improved in both groups (21 versus 19%), ns

III) Effectiveness on fatigue

Study	During/after treatment	Type of cancer	Type of exercise programme	Intensity (load)	Frequency, volume, duration	Number of patients	Outcome
Headley 2004 [71]	During chemotherapy	Breast	Home-based stretching and repeated flexion and extension exercises, video instruction	No resistance	3/week 30 minutes 2 weeks	32	EG showed significantly less increase in fatigue than CG, data NA
Houborg 2006 [72]	After surgery	Colorectal	Supervised mobilisation exercises Aerobic training Strength training Continuation at home EG compared to placebo	Not specified Not specified Weight at 50-80% of 1-RM	6/week 45 minutes during hospitalisation (≈ 10 days) and after discharge at home: ≈ 11 weeks	119	No significant differences in fatigue between groups, data NA
Mock 1997 [73]	During radiation	Breast	Home-based progressive brisk programme Walking	Self-paced	4–5/week 20–30 minutes 6 weeks	46	Fatigue decreased in EG and increased in CG, significant, data NA
Mock 2001 [74]	During radiotherapy, chemotherapy	Breast	Home-based exercise Walking	Self-paced	5–6 week 15–30 minutes 6 weeks to 6 months during cancer treatment	52	Fatigue decreased significantly more in HW (i.e. patients who walked >90 minutes per week) (-14%) compared to LW (increase of 37%)

III) Effectiveness on fatigue

Study	During/after treatment	Type of cancer	Type of exercise programme	Intensity (load)	Frequency, volume, duration	Number of patients	Outcome
Mock 2005 [75]	During radiotherapy, chemotherapy	Breast	Home-based exercise Brisk walking	50–70% MHR	5–6 /week 15–30 min 6 weeks	119	No differences in fatigue between EG and CG due to dilution of treatment Fatigue increased significantly more in non-compliers than in full compliers and more in low walkers (77%) than in high walkers (20%)
Pinto 2005 [76]	After radiation, surgery and chemo-therapy	Breast	Home-based exercise Walking, biking, swimming, counselling and pedometers	55–65% MHR	2–5/week 10–30 minutes 12 weeks	68	More reduction in fatigue in EG (36%) compared to controls (1.4%)
Segal 2003 [77]	During hormone therapy	Prostate	Supervised resistance exercise	60–70% of 1-RM, increase of 0.5 lb when >12 repetitions were completed	3/week 2 sets 8–12 repetitions, 9 exercises 12 weeks	155	EG showed improvement in fatigue during daily living activities (2%) compared to WCG that showed a decline in fatigue (-5%)
Thorsen 2005 [68]	After chemotherapy	Mixed cancer diagnosis	Supervised home-based aerobic programme Walking and cycling	Borg on 13-15 60–70% MHR	Minimal 2/week, more allowed At least 30 minutes 14 weeks	139	Fatigue decreased more in CG (40%) compared to EG (15%)
Windsor 2004 [78]	During radiotherapy	Prostate	Home-based aerobic exercise Walking	60–70% MHR	3/week 30 minutes 4 weeks	66	Fatigue increased in CG and ≈ in EG during RT, data NA

IV) Effectiveness on physical (role) functioning/ functional wellbeing/activity level							
Study	During/after treatment	Type of cancer	Type of exercise programme	Intensity (load)	Frequency, volume, duration	Number of patients	Outcome
Burnham 2002 [58]	After surgery, radiation, surgery	Mixed	Low intensity aerobic exercise Moderate-high intensity exercise treadmill Cycling	25–40% HRR 40–60% HRR	3/week 14–32 minutes 10 weeks	21	Combined exercise groups showed significant increase in QoL (9.4%) in EG compared to CG (-1.9%) Energy measure improved significantly in EG (-16%) compared to control (3.5%)
Campbell 2005 [69]	During adjuvant chemotherapy, radiotherapy, combined	Breast	Supervised aerobic training Walking and cycling Muscle-strengthening exercises	60–70% MHR (age adjusted) Muscle strengthening not specified	2/week 10–20 minutes 12 weeks	22	EG showed significantly more improvement than CG in walking distance (32% versus -5%) and in physical activity (103% versus 1.2%) and in QoL (17% versus - 4%).
Courneya 2003 [59]	After surgery, receiving adjuvant therapy	Colorectal	Home-based aerobic exercise Walking and cycling	50–75 % MHR	3–5/week 10–30 minutes 16 weeks	102	No differences between groups Patients who improved in fitness showed more improvement (4%) than decreased fitness group (-2%)
Courneya 2003 [60]	After surgery, radiation, chemotherapy	Breast	Supervised aerobic exercise Cycling	70–75% VO2max	3/week 15–35 minutes 15 weeks	53	Increase in physical wellbeing in EG (8%) compared to (W)CG (-.8%)
Hayes 2003 [79]	After chemotherapy and PBSCT	Mixed lymphatic cancer diagnoses	Aerobic exercise treadmill Walking and cycling Resistance training	70–90% MHR Weight set to induce failure between 8–20 repetitions	3/week 2/week 20–40 minutes 3 months	12	Physical QoL improved (20%) in EG and not in CG

IV) Effectiveness on physical (role) functioning/ functional wellbeing/activity level							
Study	During/after treatment	Type of cancer	Type of exercise programme	Intensity (load)	Frequency, volume, duration	Number of patients	Outcome
Headley 2004 [71]	During chemotherapy		Stretching and repeated flexion and extension exercises	No resistance	3/week 30 minutes 12 weeks	32	EG showed significantly less decline in physical wellbeing compared to CG during CT, data NA
Herrero 2006 [63]	After surgery and radiotherapy	Breast	Supervised aerobic exercise Cycling on ergometer Resistance training	70–80 % MHR Weight that allowed 12–15 repetitions, than adjusted to 8–10 repetitions, followed by an increase of 5–10%	3/week 70 minutes (20–30 minutes aerobic) 11 exercises 15 repetitions 3 sets 8 weeks	16	EG showed an increase in physical function (7%) and no change in CG
Houborg 2006 [72]	After surgery	Colorectal	Supervised mobilisation exercises aerobic training Strength training Continuation at home EG compared to placaebo	Not specified Not specified Weight at 50-80% of 1-RM	6/week 45 minutes during hospitalisation (≈ 10 days) and after discharge at home: ≈ 11 weeks	119	All indices of physical function decreased postoperative day seven and returned to preoperative level 90 days post operatively, with no significant differences between groups, data NA
Kim 2006 [64]	During chemotherapy or radiotherapy	Breast	Supervised aerobic exercise Cycling, walking, running	60-70% VO2 max	3/week 30 minutes 8 weeks	41	No between group changes Significant increase in EG compared to CG in voluntary exercise (31%versus 4%) and in energy expenditure (31versus 4%) and a decrease in sedentary activity (-12% versus - 6%)

IV) Effectiveness on physical (role) functioning/ functional wellbeing/activity level

Study	During/after treatment	Type of cancer	Type of exercise programme	Intensity (load)	Frequency, volume, duration	Number of patients	Outcome
Mock 1997 [73]	During radiation	Breast	Home-based progressive Brisk walking	Self-paced	4–5/week 20–30 minutes 6 weeks	46	EG showed significantly higher scores on 12 min WD (4%) compared to CG (-5%)
Mock 2001 [74]	During radiotherapy, chemotherapy	Breast	Home-based exercise Walking	Self-paced	5–6 week 15–30 minutes 6 weeks to 6 month during cancer treatment	52	HW (i.e. patients who walked >90 minutes per week) showed significantly higher scores than LW on functional ability (12 min WD: 6% versus -0.3%) and on self-reported physical activity (39% versus -38%) than LW. Physical functioning decreased significantly more in LW (45%) compared to HW (16%)
Mock 2005 [75]	During radiotherapy or chemotherapy	Breast	Home-based aerobic exercise Brisk walking	50–70% MHR	5–6 /week 15–30 min 6 weeks	119	EG showed significantly higher scores on WD than CG, but no differences in physical functioning (data NA) were found HE showed higher scores than LE on walking distance (6% versus -.02%), on physical functioning (5% versus -8%) and on activity levels (34% versus -14%)

IV) Effectiveness on physical (role) functioning/ functional wellbeing/activity level

Study	During/after treatment	Type of cancer	Type of exercise programme	Intensity (load)	Frequency, volume, duration	Number of patients	Outcome
Ohira 2006 [80]	After radiotherapy surgery chemo-therapy	Breast cancer	Supervised weight training Followed by own weight training	Resistance machines and free weights not specified	2/week 9 exercises 26 weeks	86	Physical global score improved by 2.1% in EG compared with a worsening by 1.2% in CG
Pinto 2003 [81]	After surgery, radio-therapy, chemo-therapy over the past 3 years	Breast (sedentary)	Supervised aerobic exercise Treadmill walking, cycling Strength training	60–70% MHR Weight 1–5lb	3/week 30 minutes 12 weeks	24	EG showed 8% reduction in heart rate at 75W, controls were not measured Changes in self-reported condition were higher (31%) in EG than in CG (-19%)
Pinto 2005 [76]	After radiation, surgery and chemo-therapy	Breast	Home-based cardiovascular exercise Walking, biking, swimming, counselling and pedometers	55–65% MHR	2–5/week 10–30 minutes 12 weeks	68	EG reported higher scores than CG on walking speed (6% versus 1%), on physical activity level (142% versus 6%) and on energy expenditure (7% versus 0.5%)
Segal 2001 [67]	During radiotherapy, chemotherapy hormonal therapy	Breast	Cardiovascular self-directed programme Walking Versus supervised programme and usual care	50–60% VO2max	5/week self-directed group 3/week supervised group 2 days at home no specification of duration 26 weeks	123	Increase in physical functioning in self-directed group (7.5%) and in supervised group (3.5%) and a decrease in usual care

IV) Effectiveness on physical (role) functioning/ functional wellbeing/activity level							
Study	During/after treatment	Type of cancer	Type of exercise programme	Intensity (load)	Frequency, volume, duration	Number of patients	Outcome
Segal 2003 [77]	During hormone therapy	Prostate	Supervised resistance exercise	60–70% of 1-RM, increase of 0.5 lb when >12 repetitions were completed	3/week 2 sets 8–12 repetitions 9 exercises 12 weeks	155	Improvement in functioning in EG (2%) compared to WCG that showed a decline (3%)
Thorsen 2005 [68]	After chemotherapy	Mixed cancer diagnosis	Home-based aerobic programme, Walking and cycling.	Borg 13-15 60–70% MHR	Minimal 2/week, more were allowed At least 30 minutes 14 weeks	139	No differences in physical function (QoL) between EG (15%) and CG (14%)
Windsor 2004 [78]	During radiotherapy	Prostate	Home-based aerobic exercise Walking	60–70% MHR	3/week 30 minutes 4 weeks	66	13.2% increase in walking distance (shuttle run test) in EG and a decrease (2.4%) in CG

Abbreviations

HRR = heart rate reserve; MHR = maximal heart hate; VO2max = maximal oxygen uptake; QoL = quality of life; EG = exercise group; (W)CG = (waiting list) control group; RG = relaxation group; PA= physical activity; PBSCT = peripheral blood stem cell transplantation; CML = chronic myeloid leukaemia; AML = acute myeloid leukaemia; NHL = non-Hodgkin's lymphoma; MDS = myelodysplastic syndrome; UE = upper extremity; LE = lower extremity; RM = repetition maximum; SLBE = Symptom Limited Bicycle Ergometry; HW = high walkers; LW = low walkers; RT = radiotherapy; CT = chemotherapy; WD = walking distance; N.S. = non significant; NA = no pre-or post intervention data available. If exact pre and post-intervention data were available changes were expressed in % of baseline scores.

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